



Clinical trial results:

A Single-Dose Study to Assess the Pharmacokinetics, Pharmacodynamics, Safety, and Tolerability of Odanacatib in Adolescents and Young Adults Treated with Glucocorticoids Summary

EudraCT number	2012-003414-14
Trial protocol	Outside EU/EEA IT GB FI
Global end of trial date	14 July 2016

Results information

Result version number	v1 (current)
This version publication date	18 February 2017
First version publication date	18 February 2017

Trial information

Trial identification

Sponsor protocol code	MK-0822-066
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01630616
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Merck Sharp & Dohme Corp.
Sponsor organisation address	2000 Galloping Hill Road, Kenilworth, NJ, United States, 07033
Public contact	Clinical Trials Disclosure, Merck Sharp & Dohme Corp., ClinicalTrialsDisclosure@merck.com
Scientific contact	Clinical Trials Disclosure, Merck Sharp & Dohme Corp., ClinicalTrialsDisclosure@merck.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMA-001123-PIP01-11
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	14 July 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	14 July 2016
Global end of trial reached?	Yes
Global end of trial date	14 July 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

This study will assess the safety, tolerability, pharmacodynamics, and pharmacokinetics of single doses of odanacatib in mature adolescents and young adults who are currently receiving glucocorticoid therapy. The primary hypotheses of the study are that a single dose of odanacatib is well tolerated in mature adolescents and that following single dose administration of odanacatib 50 mg, there is no clinically important difference in area under the drug-plasma curve from Time 0 to infinity (AUC_{0-∞}) between mature adolescents and young adults.

Protection of trial subjects:

This study was conducted in conformance with Good Clinical Practice standards and applicable country and/or local statutes and regulations regarding ethical committee review, informed consent, and the protection of human subjects participating in biomedical research.

Background therapy:

Participants received glucocorticoid therapy at a dose stable over the course of the study period and through the poststudy visit. The dose of glucocorticoids 4.5 mg/day, of prednisone or equivalent, other glucocorticoids at the discretion of the investigator after consultation with the sponsor medical monitor.

Evidence for comparator: -

Actual start date of recruitment	21 March 2013
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Italy: 3
Country: Number of subjects enrolled	Korea, Republic of: 6
Country: Number of subjects enrolled	Moldova, Republic of: 5
Country: Number of subjects enrolled	United Kingdom: 2
Country: Number of subjects enrolled	United States: 3
Worldwide total number of subjects	19
EEA total number of subjects	5

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0

Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	11
Adults (18-64 years)	8
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Recruitment continued until the Odanacatib Development Program was discontinued on 02-Sep-2016. No participants were actively receiving treatment at the time of study discontinuation.

Pre-assignment

Screening details:

The participant was a male or female between the ages of 12 and 17 years of age (inclusive) for adolescents or a male or female between the ages of 18-25 years of age (inclusive) for young adults.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	Adolescents Odanacatib 10 mg

Arm description:

Study drug (single oral dose of odanacatib 10 mg) was administered following at least an 8-hour fast to adolescents.

Arm type	Experimental
Investigational medicinal product name	Odanacatib
Investigational medicinal product code	
Other name	MK-0822
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Study drug (single oral dose of odanacatib 10 mg) was administered following at least an 8-hour fast. The dose was given with 240 mL of water.

Arm title	Adolescents Odanacatib 50 mg
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Arm description:

Study drug (single oral dose of odanacatib 50 mg) was administered following at least an 8-hour fast to adolescents.

Arm type	Experimental
Investigational medicinal product name	Odanacatib
Investigational medicinal product code	
Other name	MK-0822
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Study drug (single oral dose of odanacatib 50 mg) was administered following at least an 8-hour fast. The dose was given with 240 mL of water.

Arm title	Adolescents Placebo
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Arm description:

Study drug (single oral dose of placebo) was administered following at least an 8-hour fast to adolescents.

Arm type	Placebo
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Investigational medicinal product name	Placebo to odanacatib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Study drug (single oral dose of placebo) was administered following at least an 8-hour fast. The dose was given with 240 mL of water.

Arm title	Young Adults Odanacatib 50 mg
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Arm description:

Study drug (single oral dose of odanacatib 50 mg) was administered following at least an 8-hour fast to young adults.

Arm type	Experimental
Investigational medicinal product name	Odanacatib
Investigational medicinal product code	
Other name	MK-0822
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Study drug (single oral dose of odanacatib 50 mg) was administered following at least an 8-hour fast. The dose was given with 240 mL of water.

Arm title	Young Adults Placebo
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Arm description:

Study drug (single oral dose of placebo) was administered following at least an 8-hour fast to young adults.

Arm type	Placebo
Investigational medicinal product name	Placebo to odanacatib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Study drug (single oral dose of placebo) was administered following at least an 8-hour fast. The dose was given with 240 mL of water.

Number of subjects in period 1	Adolescents Odanacatib 10 mg	Adolescents Odanacatib 50 mg	Adolescents Placebo
Started	5	3	3
Completed	5	3	3

Number of subjects in period 1	Young Adults Odanacatib 50 mg	Young Adults Placebo
Started	6	2
Completed	6	2

Baseline characteristics

Reporting groups

Reporting group title	Adolescents Odanacatib 10 mg
Reporting group description: Study drug (single oral dose of odanacatib 10 mg) was administered following at least an 8-hour fast to adolescents.	
Reporting group title	Adolescents Odanacatib 50 mg
Reporting group description: Study drug (single oral dose of odanacatib 50 mg) was administered following at least an 8-hour fast to adolescents.	
Reporting group title	Adolescents Placebo
Reporting group description: Study drug (single oral dose of placebo) was administered following at least an 8-hour fast to adolescents.	
Reporting group title	Young Adults Odanacatib 50 mg
Reporting group description: Study drug (single oral dose of odanacatib 50 mg) was administered following at least an 8-hour fast to young adults.	
Reporting group title	Young Adults Placebo
Reporting group description: Study drug (single oral dose of placebo) was administered following at least an 8-hour fast to young adults.	

Reporting group values	Adolescents Odanacatib 10 mg	Adolescents Odanacatib 50 mg	Adolescents Placebo
Number of subjects	5	3	3
Age Categorical Units: Subjects			
Adolescents (12-17 years)	5	3	3
Adults (18-64 years)	0	0	0
Age Continuous Units: years			
arithmetic mean	14.8	15.7	16.3
standard deviation	± 1.6	± 0.6	± 0.6
Gender Categorical Units: Subjects			
Female	4	2	1
Male	1	1	2

Reporting group values	Young Adults Odanacatib 50 mg	Young Adults Placebo	Total
Number of subjects	6	2	19
Age Categorical Units: Subjects			
Adolescents (12-17 years)	0	0	11
Adults (18-64 years)	6	2	8
Age Continuous Units: years			
arithmetic mean	22.3	20	-
standard deviation	± 1.6	± 0	-

Gender Categorical Units: Subjects			
Female	3	2	12
Male	3	0	7

Subject analysis sets

Subject analysis set title	Young Adults Odanacatib 10 mg
Subject analysis set type	Full analysis

Subject analysis set description:

Study drug (single oral dose of odanacatib 10 mg) was administered following at least an 8-hour fast to young adults. Historical data from study MK-0822-007.

Reporting group values	Young Adults Odanacatib 10 mg		
Number of subjects	9		
Age Categorical Units: Subjects			
Adolescents (12-17 years)	0		
Adults (18-64 years)	9		
Age Continuous Units: years arithmetic mean standard deviation	\pm		
Gender Categorical Units: Subjects			
Female	8		
Male	1		

End points

End points reporting groups

Reporting group title	Adolescents Odanacatib 10 mg
Reporting group description: Study drug (single oral dose of odanacatib 10 mg) was administered following at least an 8-hour fast to adolescents.	
Reporting group title	Adolescents Odanacatib 50 mg
Reporting group description: Study drug (single oral dose of odanacatib 50 mg) was administered following at least an 8-hour fast to adolescents.	
Reporting group title	Adolescents Placebo
Reporting group description: Study drug (single oral dose of placebo) was administered following at least an 8-hour fast to adolescents.	
Reporting group title	Young Adults Odanacatib 50 mg
Reporting group description: Study drug (single oral dose of odanacatib 50 mg) was administered following at least an 8-hour fast to young adults.	
Reporting group title	Young Adults Placebo
Reporting group description: Study drug (single oral dose of placebo) was administered following at least an 8-hour fast to young adults.	
Subject analysis set title	Young Adults Odanacatib 10 mg
Subject analysis set type	Full analysis
Subject analysis set description: Study drug (single oral dose of odanacatib 10 mg) was administered following at least an 8-hour fast to young adults. Historical data from study MK-0822-007.	

Primary: Number of Participants Who Report an Adverse Event (AE)

End point title	Number of Participants Who Report an Adverse Event (AE) ^[1]
End point description: An AE is defined as any unfavorable and unintended sign including an abnormal laboratory finding, symptom or disease associated with the use of a medical treatment or procedure, regardless of whether it is considered related to the medical treatment or procedure, that occurs during the course of the study. The primary population for safety analysis was the Full Analysis Set (FAS) population which consisted of all randomized participants who received at least 1 dose of study drug.	
End point type	Primary
End point timeframe: Up to Day 14	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: No statistical analyses were planned or performed for this primary end point.

End point values	Adolescents Odanacatib 10 mg	Adolescents Odanacatib 50 mg	Adolescents Placebo	Young Adults Odanacatib 50 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	3	3	6
Units: Participants	1	0	0	1

End point values	Young Adults Placebo			
Subject group type	Reporting group			
Number of subjects analysed	2			
Units: Participants	0			

Statistical analyses

No statistical analyses for this end point

Primary: Area Under the Plasma-Drug Concentration Time Curve from Hour 0 to Infinity (AUC0-inf) for Adolescents and Young Adults Following a Single Oral Dose of Odanacatib 50 mg

End point title	Area Under the Plasma-Drug Concentration Time Curve from Hour 0 to Infinity (AUC0-inf) for Adolescents and Young Adults Following a Single Oral Dose of Odanacatib 50 mg ^{[2][3]}
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End point description:

The primary analysis dataset included all participants who were compliant with the protocol sufficiently to ensure that these data would likely exhibit the effects of treatment, according to the underlying scientific model, and had available data from at least one treatment.

End point type	Primary
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End point timeframe:

Hour 0 (predose), and at 1, 2, 6, 8, 24, 96, 168, 240, and 336 hours post-dose

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: No statistical analyses were planned or performed for this primary end point.

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: No statistical analyses were planned or performed for this primary end point.

End point values	Adolescents Odanacatib 50 mg	Young Adults Odanacatib 50 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3	6		
Units: µM·hr				
geometric mean (geometric coefficient of variation)	21.6 (± 30.7)	27.2 (± 40.4)		

Statistical analyses

No statistical analyses for this end point

Primary: Area Under the Plasma-Drug Concentration Time Curve from Hour 0 to 168 hours (AUC0-168) For Adolescents and Young Adults Following a Single Oral Dose of Odanacatib 50 mg

End point title	Area Under the Plasma-Drug Concentration Time Curve from Hour 0 to 168 hours (AUC0-168) For Adolescents and Young Adults Following a Single Oral Dose of Odanacatib 50 mg ^{[4][5]}
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End point description:

The primary analysis dataset included all participants who were compliant with the protocol sufficiently to ensure that these data would likely exhibit the effects of treatment, according to the underlying scientific model, and had available data from at least one treatment.

End point type	Primary
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End point timeframe:

Hour 0 (predose), and at 1, 2, 6, 8, 24, 96, 168, 240, and 336 hours post-dose

Notes:

[4] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: No statistical analyses were planned or performed for this primary end point.

[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: No statistical analyses were planned or performed for this primary end point.

End point values	Adolescents Odanacatib 50 mg	Young Adults Odanacatib 50 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3	6		
Units: $\mu\text{M}\cdot\text{hr}$				
geometric mean (geometric coefficient of variation)	18.7 (\pm 24)	21.5 (\pm 39.8)		

Statistical analyses

No statistical analyses for this end point

Primary: Maximum Plasma Concentration (C_{max}) of Odanacatib For Adolescents and Young Adults Following a Single Oral Dose of Odanacatib 50 mg

End point title	Maximum Plasma Concentration (C _{max}) of Odanacatib For Adolescents and Young Adults Following a Single Oral Dose of Odanacatib 50 mg ^{[6][7]}
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End point description:

The primary analysis dataset included all participants who were compliant with the protocol sufficiently to ensure that these data would likely exhibit the effects of treatment, according to the underlying scientific model, and had available data from at least one treatment. C_{max} is a measure of the maximum amount of drug in the plasma after the dose is given.

End point type	Primary
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End point timeframe:

Hour 0 (predose), and at 1, 2, 6, 8, 24, 96, 168, 240, and 336 hours post-dose

Notes:

[6] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: No statistical analyses were planned or performed for this primary end point.

[7] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: No statistical analyses were planned or performed for this primary end point.

End point values	Adolescents Odanacatib 50 mg	Young Adults Odanacatib 50 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3	6		
Units: nM				
geometric mean (geometric coefficient of variation)	256 (± 30.8)	237 (± 51.1)		

Statistical analyses

No statistical analyses for this end point

Primary: Time to Cmax (Tmax) of Odanacatib For Adolescents and Young Adults Following a Single Oral Dose of Odanacatib 50 mg

End point title	Time to Cmax (Tmax) of Odanacatib For Adolescents and Young Adults Following a Single Oral Dose of Odanacatib 50 mg ^[8] ^[9]
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End point description:

Tmax is the time required to reach Cmax. The primary analysis dataset included all participants who were compliant with the protocol sufficiently to ensure that these data would likely exhibit the effects of treatment, according to the underlying scientific model, and had available data from at least one treatment.

End point type	Primary
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End point timeframe:

Hour 0 (predose), and at 1, 2, 6, 8, 24, 96, 168, 240, and 336 hours post-dose

Notes:

[8] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: No statistical analyses were planned or performed for this primary end point.

[9] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: No statistical analyses were planned or performed for this primary end point.

End point values	Adolescents Odanacatib 50 mg	Young Adults Odanacatib 50 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3	6		
Units: Hours				
median (full range (min-max))	6 (2 to 24)	9 (1 to 24)		

Statistical analyses

No statistical analyses for this end point

Primary: Apparent Terminal Half-life (t1/2) of Odanacatib For Adolescents and Young Adults Following a Single Oral Dose of Odanacatib 50 mg

End point title	Apparent Terminal Half-life (t1/2) of Odanacatib For Adolescents and Young Adults Following a Single Oral Dose of Odanacatib 50 mg ^[10] ^[11]
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End point description:

The primary analysis dataset included all participants who were compliant with the protocol sufficiently to ensure that these data would likely exhibit the effects of treatment, according to the underlying scientific model, and had available data from at least one treatment.

End point type	Primary
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End point timeframe:

Hour 0 (predose), and at 1, 2, 6, 8, 24, 96, 168, 240, and 336 hours post-dose

Notes:

[10] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: No statistical analyses were planned or performed for this primary end point.

[11] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: No statistical analyses were planned or performed for this primary end point.

End point values	Adolescents Odanacatib 50 mg	Young Adults Odanacatib 50 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3	6		
Units: Hours				
geometric mean (geometric coefficient of variation)	66.9 (± 30.4)	77.3 (± 20.9)		

Statistical analyses

No statistical analyses for this end point

Primary: AUC0-inf for Adolescents and Young Adults Following a Single Oral Dose of Odanacatib 10 mg

End point title	AUC0-inf for Adolescents and Young Adults Following a Single Oral Dose of Odanacatib 10 mg ^[12]
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End point description:

The AUC0-inf data for 10-mg odanacatib in adolescents were compared with the historical young adult AUC0-inf data from study MK-0822-007. The primary analysis dataset included all participants who were compliant with the protocol sufficiently to ensure that these data would likely exhibit the effects of treatment, according to the underlying scientific model, and had available data from at least one treatment.

End point type	Primary
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End point timeframe:

Hour 0 (predose), and at 1, 2, 6, 8, 24, 96, 168, 240, and 336 hours post-dose

Notes:

[12] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: No statistical analyses were planned or performed for this primary end point.

End point values	Adolescents Odanacatib 10 mg	Young Adults Odanacatib 10 mg		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	5	9		
Units: µM·hr				
geometric mean (confidence interval 95%)	10 (7.5 to 13.3)	11.3 (9.1 to 13.9)		

Statistical analyses

Statistical analysis title	Ratio (Adolescents/adults)
Comparison groups	Adolescents Odanacatib 10 mg v Young Adults Odanacatib 10 mg
Number of subjects included in analysis	14
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Ratio (Adolescents/adults)
Point estimate	0.89
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.62
upper limit	1.26

Primary: AUC0-168 For Adolescents and Young Adults Following a Single Oral Dose of Odanacatib 10 mg

End point title	AUC0-168 For Adolescents and Young Adults Following a Single Oral Dose of Odanacatib 10 mg ^[13]
End point description:	The AUC0-168 data for 10-mg odanacatib in adolescents were compared with the historical young adult AUC0-168 data from study MK-0822-007. The primary analysis dataset included all participants who were compliant with the protocol sufficiently to ensure that these data would likely exhibit the effects of treatment, according to the underlying scientific model, and had available data from at least one treatment.
End point type	Primary
End point timeframe:	Hour 0 (predose), and at 1, 2, 6, 8, 24, 96, 168, 240, and 336 hours post-dose

Notes:

[13] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: No statistical analyses were planned or performed for this primary end point.

End point values	Adolescents Odanacatib 10 mg	Young Adults Odanacatib 10 mg		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	5	9		
Units: $\mu\text{M}\cdot\text{hr}$				
geometric mean (confidence interval 95%)	8.1 (6.2 to 10.7)	9.3 (7.6 to 11.4)		

Statistical analyses

Statistical analysis title	Ratio (Adolescents/Adults)
Comparison groups	Adolescents Odanacatib 10 mg v Young Adults Odanacatib 10 mg
Number of subjects included in analysis	14
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Ratio (Adolescents/Adults)
Point estimate	0.87
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.62
upper limit	1.23

Primary: Cmax of Odanacatib For Adolescents and Young Adults Following a Single Oral Dose of Odanacatib 10 mg

End point title	Cmax of Odanacatib For Adolescents and Young Adults Following a Single Oral Dose of Odanacatib 10 mg ^[14]
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End point description:

The Cmax data for 10-mg odanacatib in adolescents were compared with the historical young adult Cmax data from study MK-0822-007. The primary analysis dataset included all participants who were compliant with the protocol sufficiently to ensure that these data would likely exhibit the effects of treatment, according to the underlying scientific model, and had available data from at least one treatment.

End point type	Primary
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End point timeframe:

Hour 0 (predose), and at 1, 2, 6, 8, 24, 96, 168, 240, and 336 hours post-dose

Notes:

[14] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: No statistical analyses were planned or performed for this primary end point.

End point values	Adolescents Odanacatib 10 mg	Young Adults Odanacatib 10 mg		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	5	9		
Units: nM				
geometric mean (confidence interval 95%)	99.6 (75 to 132.4)	122.3 (99 to 151.1)		

Statistical analyses

Statistical analysis title	Ratio (Adolescents/Adults)
Comparison groups	Adolescents Odanacatib 10 mg v Young Adults Odanacatib 10 mg
Number of subjects included in analysis	14
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Ratio (Adolescents/Adults)
Point estimate	0.81
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.57
upper limit	1.16

Primary: Tmax of Odanacatib For Adolescents and Young Adults Following a Single Oral Dose of Odanacatib 10 mg

End point title	Tmax of Odanacatib For Adolescents and Young Adults Following a Single Oral Dose of Odanacatib 10 mg ^{[15][16]}
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End point description:

Tmax is the time required to reach Cmax. The Tmax data for 10-mg odanacatib in adolescents were compared with the historical young adult Tmax data from study MK-0822-007. The primary analysis dataset included all participants who were compliant with the protocol sufficiently to ensure that these data would likely exhibit the effects of treatment, according to the underlying scientific model, and had available data from at least one treatment.

End point type	Primary
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End point timeframe:

Hour 0 (predose), and at 1, 2, 6, 8, 24, 96, 168, 240, and 336 hours post-dose

Notes:

[15] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: No statistical analyses were planned or performed for this primary end point.

[16] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: No statistical analyses were planned or performed for this primary end point.

End point values	Adolescents Odanacatib 10 mg	Young Adults Odanacatib 10 mg		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	5	9		
Units: Hours				
median (full range (min-max))	6 (6 to 24)	6 (4 to 32)		

Statistical analyses

No statistical analyses for this end point

Primary: t1/2 of Odanacatib For Adolescents and Young Adults Following a Single Oral Dose of Odanacatib 10 mg

End point title	t1/2 of Odanacatib For Adolescents and Young Adults Following a Single Oral Dose of Odanacatib 10 mg ^{[17][18]}
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End point description:

The t1/2 data for 10-mg odanacatib in adolescents were compared with the historical young adult t1/2 data from study MK-0822-007. The primary analysis dataset included all participants who were compliant with the protocol sufficiently to ensure that these data would likely exhibit the effects of treatment, according to the underlying scientific model, and had available data from at least one treatment.

End point type	Primary
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End point timeframe:

Hour 0 (predose), and at 1, 2, 6, 8, 24, 96, 168, 240, and 336 hours post-dose

Notes:

[17] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: No statistical analyses were planned or performed for this primary end point.

[18] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: No statistical analyses were planned or performed for this primary end point.

End point values	Adolescents Odanacatib 10 mg	Young Adults Odanacatib 10 mg		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	5	9		
Units: Hours				
geometric mean (geometric coefficient of variation)	80.5 (± 17.9)	73 (± 23.4)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Inhibition of Urinary Aminoterminal Crosslinked Telopeptide of Type 1 Collagen (uNTx/Cr) to 168 Hours Postdose

End point title	Change from Baseline in Inhibition of Urinary Aminoterminal Crosslinked Telopeptide of Type 1 Collagen (uNTx/Cr) to 168 Hours Postdose
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End point description:

Urinary aminoterminal crosslinked telopeptide of Type I collagen (uNTx/Cr) is a biochemical marker of bone resorption. The primary analysis dataset included all participants who were compliant with the protocol sufficiently to ensure that these data would likely exhibit the effects of treatment, according to the underlying scientific model, and had available data from at least one treatment.

End point type	Secondary
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End point timeframe:

Baseline (predose Day 1) and 168 hours postdose

End point values	Adolescents Odanacatib 10 mg	Adolescents Odanacatib 50 mg	Adolescents Placebo	Young Adults Odanacatib 50 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	3	3	6
Units: nmol[BCE]/mmol[creatinine])				
geometric mean (geometric coefficient of variation)	0.79 (± 50.68)	0.4 (± 232)	1.03 (± 3.39)	0.36 (± 53.62)

End point values	Young Adults Placebo			
Subject group type	Reporting group			
Number of subjects analysed	2			
Units: nmol[BCE]/mmol[creatinine])				
geometric mean (geometric coefficient of variation)	0.83 (± 13.53)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to 14 days

Adverse event reporting additional description:

The primary population for safety analysis was the FAS population which consisted of all randomized participants who received at least 1 dose of study drug.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	19.1
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Reporting groups

Reporting group title	Adolescents Odanacatib 10 mg
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Reporting group description:

Study drug (single oral dose of odanacatib 10 mg) was administered following at least an 8-hour fast.

Reporting group title	Adolescents Odanacatib 50 mg
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Reporting group description:

Study drug (single oral dose of odanacatib 50 mg) was administered following at least an 8-hour fast.

Reporting group title	Adolescents Placebo
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Reporting group description:

Study drug (single oral dose of placebo) was administered following at least an 8-hour fast.

Reporting group title	Young Adults Odanacatib 50 mg
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Reporting group description:

Study drug (single oral dose of odanacatib 50 mg) was administered following at least an 8-hour fast.

Reporting group title	Young Adults Placebo
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Reporting group description:

Study drug (single oral dose of placebo) was administered following at least an 8-hour fast.

Serious adverse events	Adolescents Odanacatib 10 mg	Adolescents Odanacatib 50 mg	Adolescents Placebo
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 5 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0

Serious adverse events	Young Adults Odanacatib 50 mg	Young Adults Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Adolescents Odanacatib 10 mg	Adolescents Odanacatib 50 mg	Adolescents Placebo
Total subjects affected by non-serious adverse events subjects affected / exposed	1 / 5 (20.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
Investigations Blood potassium increased subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 1	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0
Renal and urinary disorders Nephrotic syndrome subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 1	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0
Musculoskeletal and connective tissue disorders Systemic lupus erythematosus subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0

Non-serious adverse events	Young Adults Odanacatib 50 mg	Young Adults Placebo	
Total subjects affected by non-serious adverse events subjects affected / exposed	1 / 6 (16.67%)	0 / 2 (0.00%)	
Investigations Blood potassium increased subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 2 (0.00%) 0	
Renal and urinary disorders Nephrotic syndrome subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 2 (0.00%) 0	
Musculoskeletal and connective tissue disorders Systemic lupus erythematosus subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1	0 / 2 (0.00%) 0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
18 November 2013	AM1 - Addition of Panel C (participants receiving a single oral dose of odanacatib 50 mg or placebo 8 participants (6 active 2 placebo), 18 to 25 years of age and reduction in the duration of prior concomitant therapy with glucocorticoid.
02 May 2014	AM3 - Modified sample criteria: attempt to enroll at least 2 rather than 3 of each gender at each dose level and changes to some PK/PD time points.
17 September 2015	AM5 - The diet plan was modified and fasting requirements were added for pharmacokinetic and pharmacodynamic sampling. The washout periods for the prior therapy with cyclosporine and bisphosphonates were reduced. Oral contraceptive use was now permitted. Instruction for use of the emergency unblinding call center was added.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

This study was terminated early due to the discontinuation of the Odanacatib Development Program on 02-Sep-2016 and only a small number of participants were enrolled. The number of PK time points was reduced to 8 to 11 per Ethics Committee requests.

Notes: